PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NL2004/000018	09.01.2004	

International Patent Classification (IPC) or both national classification and IPC
C07C209/50, C07D295/02, B01J23/26, B01J23/28, B01J23/36, B01J23/60, B01J23/62, B01J23/64, B01J23/80,

Applicant
AVANTIUM INTERNATIONAL B.V.

1. This opinion contains indications relating to the following items:

- ☒ Box No I Basis of the opinion
- ☒ Box No II Priority
- ☒ Box No III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No IV Lack of unity of invention
- ☒ Box No V Reasoned statement under Rule 43*bis* 1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No VI Certain documents cited
- ☐ Box No VII Certain defects in the international application
- ☒ Box No VIII Certain observations on the international application

2 **FURTHER ACTION**

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220

3. For further details, see notes to Form PCT/ISA/220

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Veefkind, V

Telephone No +31 70 340-1017

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/NL2004/000018

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-27 (in part), 28-31

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1-27 (in part), 28-31

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. Invention 1: claims 1-27 (in part)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	8,9,11-20 (in part)
	No:	Claims	1-7,10,25-27 (in part)
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-27 (in part)
Industrial applicability (IA)	Yes:	Claims	1-27 (in part)
	No:	Claims	

2. Citations and explanations

   see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.
PCT/NL2004/000018

Reference is made to the following documents:

D1: US-A-4 035 353 (KANETAKA JUNICHI ET AL) 12 July 1977 (1977-07-12)

D2: HIROSAWA C ET AL: "Hydrogenation of Amides by the Use of Bimetallic Catalysts Consisting of Group 8 to 10, and Group 6 or 7 Metals" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 37, no. 37, 9 September 1996 (1996-09-09), pages 6749-6752, XP004088084 ISSN: 0040-4039

D3: EP-A-0 286 280 (BP CHEM INT LTD) 12 October 1988 (1988-10-12)

D4: US-A-4 772 750 (HABERMANN CLARENCE E) 20 September 1988 (1988-09-20)

Re Item IV

Lack of unity of invention

A) Firstly the prior art is shortly discussed:

It is noted that according to the description (page 2, lines 14-24) of the present application the different metals need not necessarily be present as heterogeneous catalysts and that they may be present on different supports.

D1 (see claim 1) discloses a process for producing hexamethyleneimine (secondary amine) by catalytic hydrogenation of caprolactam (amide) over a Co-Mo bimetallic catalyst at a temperature of 100-350°C and a pressure from atmospheric pressure to 200 kg/cm^2. D1 destroys the novelty of claim 1. Note that D1 also discloses trimetallic Co-Re-Mo catalysts for this process.

D2 (see especially page 6749, last paragraph of page 6752 and examples) discloses different bimetallic combinations of the metals Re, Mo and W with Rh or Ru as catalysts for the hydrogenation of amides to amines under 'mild conditions'. D2, as in the present application, specifically wishes to avoid the need to high pressure and temperature associated with prior art catalysts. The examples are performed at 160°C and 100 atm.

The difference between D2 and claim 1 is a lowering of the pressure (which for many catalysts in the application results in yields at 160°C which are (far) below 80%).

The problem underlying the application thus appears to be the provision of an alternative (but not necessarily better) process for hydrogenation of amides into amines, which is performed at especially mild conditions.

The solution with respect to D2 is use of a pressure below 50 bar. Knowing from the general teaching of D2 that these catalysts were especially effective for milder conditions and wishing to explore use under even milder conditions, the skilled person would have also tried to carry out the same process at a pressure of below 50 bar as a matter of routine trial end error experimentation without becoming inventive.

D3 discloses a process for the production of an amine by reacting an amide with hydrogen in the presence of a bimetallic catalyst consisting of a group VIII noble metal and Re, and a zeolite or alumina (claim 1). Suitable operating conditions are 150-300°C and 200 psig (13 bar) to 300 psig (207 bar).

D3 destroys the novelty of the subject-matter of some alternatives within claim 1, as well as of some of the alternatives in claim 25, notably PtRe and IrRe.

B) According to the PCT International Search and Examination Guidelines, Part III, 10.06 (as in force from March 25, 2004), unity of invention has to be considered in the first place only in relation to the independent claims.

There are 3 independent claims:
Independent claim 1, relating to a method for catalytic reduction of an amide at a temperature of below 200°C and a pressure of below 50 bar using a bimetallic or trimetallic catalyst.
Independent claim 25, relating to a selection of bimetallic and trimetallic catalysts.
Independent claim 28, relating to a method for the selection of at least one bi- or trimetallic catalyst, active in the reduction of amides into amines.

It appears that within these independent claims unity does not exist for the following reasons:

The "same" or "corresponding" technical features between these independent claims are "bi- or trimetallic catalysts suitable for the reduction of amides to amines"

These features are already known from D1-D3, see the above discussion

Therefore, these features are no special (new and inventive) technical features. Thus, no "same" or "corresponding" special technical features could be found between the independent claims 1,25 and 28, as required by Rule 13.2 PCT.

The problem associated with the subject-matter of claims 1 and 25 appears to be the provision of a catalyst for reduction of amides into amines which operates under especially mild conditions.

The problem associated with the subject-matter of claim 28 appears to be the provision of a methodology for effectively finding bi- or trimetallic catalyst compositions for reduction of amides into amines, but not necessarily under especially mild conditions. Such catalysts may not necessarily be provided by this method (depending on the catalysts that are prepared).

Thus, both (groups of) inventions relate to different problems. No common problem could be found (also in view of prior art D1-D3), which could serve as the general inventive concept required by Rule 13.1 PCT.
Consequently, these claims are not unitary according to Rule 13 PCT.

Thus, the application is initially split into 2 groups of (alleged) inventions:

Group I: claims 1-27
Group II: claims 28-31

C) Rule 13.3 PCT requires that the determination whether a group of inventions is linked so as to form a general inventive concept (Rule 13.1 PCT) shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

Both independent claim 1 as well as independent claim 25 deal with a number of alternatives within the same claim (i.e. "Markush").

The "same" or "corresponding" technical features between these alternatives are "bi- or trimetallic catalysts suitable for the reduction of amides to amines"

Both bi- and trimetallic catalysts are already known for this purpose from D1-D3, see the above discussion. In addition, some of the Markush alternatives from claim 1, as well as from claim 25 are not novel and/or lack inventive step (see discussion of prior art under A))

As these features do not provide a contribution over prior art, these features are

no special (new and inventive) technical features. Thus, no "same" or "corresponding" special technical features could be found between the alternatives in claim 1 or in claim 25, as required by Rule 13.2 PCT.

The problem underlying the independent claims of providing catalysts for reduction of amides to amines, operable under milder conditions than prior art is already known from, and solved by, prior art (see discussion of D1-D3 above). Thus, no common problem could be found, which could serve as the general inventive concept required by Rule 13.1 PCT.
Consequently, these alternatives are not unitary according to Rule 13 PCT.

D) According to the PCT International Search and Examination Guidelines, Part III, Paragraph 10.17 (as in force from March 25, 2004), for Markush grouping the requirement of a technical interrelationship and the same or corresponding technical features as defined in Rule 13.2 shall be considered to be met when the alternatives are of a similar nature.

The alternatives shall be considered as being of similar nature when:

(A) All alternatives have a common property or activity, and

(B)(1) a common structure is present, that is, a significant structural element is shared by all alternatives, or

(B)(2) all alternatives belong to a recognized class of chemical compounds in the art to which the (alleged) invention pertains,

in which the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

With regards to (B)(1) and (B)(2), note that any combination of groups A, B and C is permissible, i.e., none of the groups can be regarded as a significant structural element that is shared by all alternatives. Nor can the groups A, B and C, or their content be said to belong to one recognized class of compounds.

Therefore neither of the alternative conditions (B)(1) or (B)(2) are met, and the relationship defined in Rule 13.2 is deemed not to be fulfilled.

More specifically:

Group A of claim 1 is considered to contain two groups of elements, the first one (A1) contains the first row elements of groups 8 and 9 (Co and Fe) of the Periodic

Table, the second one (A2) the specific selection of noble metals (Ir, Pt, Rh and Ru).

Group B1 contains the group 6 metals (Cr, Mo), Group B2 contains the group 7 metal Re, and group B3 the group 5 metal V.

Group C1 (Cu), C2 (In) and C3 (Zn) contain metals of groups 11, 13 and 12 of the Periodic Table, respectively.

For A1, A2; B1, B2, B3; C1, C2, C3 this result in 18 combinations ABC, 6 combinations AB, 6 combinations AC and 9 combinations BC, giving a total of 39 inventions to which the "corresponding" catalysts of claim 25 are grouped as well.

This gives the following groups:
Group I1: Claims 1-24 insofar the catalyst is chosen from A1B1C1, claims 25-27 if they comprise one or more catalysts A1B1C1.

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Group I39: Claims 1-24 insofar the catalyst is chosen from B3C3, i.e., VZn, claims 25-27 if they comprise VZn.

Group II: Claims 28-31.

Although not-unitary, the group A2B2 has been additionally searched in its entirety without requiring an additional effort and will also be examined as such, giving as final groups identified:

Group 1: Claims 1-24 insofar the catalyst is chosen from A1B1C1, claims 25-27 if they comprise one or more catalysts A1B1C1.
Claims 1-24 insofar the catalyst is chosen from A2B2, claims 25-27 if they comprise one or more catalysts A2B2.

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Group 38: Claims 1-24 insofar the catalyst is chosen from B3C3, i.e., VZn, claims 25-27 if they comprise Vzn.

Group 39: Claims 28-31.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Group A1B1C1:

Apart from the remark made under Item VIII, below, regarding support and disclosure, it would appear that the use of some of the catalysts (especially CoCrCu and FeCrCu) mentioned for the reduction of 1-acetylpyrrolidine to 1-ethylpyrrolidine and especially at the specific temperature of around 160°C is novel and that the catalysts may be considered as non-obvious alternative catalysts over D2.

Group A2B2:

The remarks under Item VIII notwithstanding, the following is remarked w.r.t. novelty (Article 33(1) and (2) PCT) and inventive step (Article 3381) and (3) PCT):

D3 discloses a process for the production of an amine by reacting an amide with hydrogen in the presence of a bimetallic catalyst consisting of a group VIII noble metal and Re, and a zeolite or alumina (claim 1). Suitable operating conditions are 150-300°C and 200 psig (13 bar) to 300 psig (207 bar). The process may be performed batchwise or continuously.

D3 destroys the novelty of the subject-matter of alternatives A2B2 in claims 1-7,10, and claims 25-27.

Additionally the subject-matter of the claims 1-27 as currently on file is regarded to lack an inventive step over D2, for the reasons as set out in Item IV, point A.

Re Item VIII
Certain observations on the international application

Group A1B1C1:

1.1 Some of the specific alternatives comprised in this group (Such as FeMoCu at 100°C (see Figure 2)), do not appear to give any activity for the one reaction for which a test result was available.

According to D2, last page, the reaction performed in this one example is a

relatively easy hydrogenation of an amide. Some lactones are much more difficult to hydrogenate to corresponding amines. No evidence for the performance of the catalysts for other hydrogenations of amides to amines has been presented.

1.2 No information at all appears to be available for the liquid phase reaction for this group. Since already not many of the other alternatives seem to work, without experimental evidence no support is considered to be present for the liquid phase reactions for this group.

As a result none of the claims 1-25 in their current form is regarded as sufficiently supported and disclosed (Articles 5 and 6 PCT) for the group A1B1C1.

group A2B2:

With regards to the liquid phase reactions, some catalysts comprising a noble metal and Re (for example Ru:Re) may give some reaction or no reaction at all, depending on their specific composition. Apparently there are essential features missing. As a result of their broad scope which is not justified by the experimental results, these claims are considered to lack support (Article 6 PCT).